UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,396	08/06/2001	Wolff M. Kirsch	LOMAU.140A	6247

5318 7590 04/21/2004

NATIONAL INSTITUTES OF HEALTH
OFFICE OF TECHNOLOGY TRANSFER
6011 EXECUTIVE BLVD SUITE 325
ROCKVILLE, MD 20852-3804

EXAMINER	
CHERNYSHEV, OLGA N	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 04/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/924,396	KIRSCH ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-9 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-9, 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 27, 2004 has been entered.

Response to Amendment

2. Claims 7 and 9 have been amended, claim 20 has been cancelled and claim 21 has been added as requested in the amendment of Paper filed on February 27, 2004. Claims 7-9 and 21 are pending in the instant application.

Claims 7-9 and 21 are under examination in the instant office action.

3. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

5. Applicant's arguments filed on February 27, 2004 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Objections

6. Claim 21 is objected to because of the following informalities: "probe-that" should be "probe that", perhaps. Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. Claims 7-9, as amended, and claim 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 7-9 are directed to a method of identifying a subject as likely to develop or have Alzheimer's disease or Mild Cognitive Impairment (MCI) by comparing amounts of probe that interacts with iron-regulatory protein-2 (IRP-2) in a sample of peripheral blood cells, wherein more probe that interacts with IRP-2 leads to identification of a subject as likely to develop or have Alzheimer's disease or Mild Cognitive Impairment (MCI). Claim 21 is directed to a method for the identification of a defect in iron metabolism in a patient by detecting more or less probe that interacts with IRP-2 in a sample of peripheral blood cells as compared to control sample. However, the instant specification fails to provide enough guidance for one skilled in the art on how to practice the instant methods, thereby requiring undue experimentation to discover how to use Applicant's invention, as currently claimed.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working

examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

The instant invention is predicated on the finding that mutations in the IRP-2 gene perturb iron homeostasis. It is further asserted that mutations in IRP-2 gene could be associated with Alzheimer's disease and MCI. The instant specification, as originally filed, contemplates two methods to diagnose Alzheimer's disease; first, by the presence of a mutated form of IRP-2 ("[t]he presence of antibody to mutant forms of IRP-2 indicates a predilection to contract a neurodegenerative disease", page 7, lines 25-26) and, second, by comparing the levels of IRP-2 protein ("[b]y monitoring the levels of mutant and wild-type IRP-2 proteins and/or the nucleic acids encoding these molecules, a prognosis of neurodegenerative disease can be made", see page 8, lines 7-8). The instant specification, as originally filed, does not disclose any specific quantitative data regarding the levels of IRP-2 predictive of Alzheimer's disease or MCI or particular mutations in IRP-2 gene as markers for Alzheimer's disease or MCI. Further, the Declaration of Kirsch under 37 CFR 1.132 filed June 12, 2003 provided microphotographs which showed that a sample of lymphocytes obtained from an Alzheimer's disease patient and stained with IRP-2 antibodies had a different pattern of staining compare to a sample of control lymphocytes (see page 2, section 5 of the Declaration and Exhibit B).

The second Declaration of Kisch under 37 CFR 1.132 filed on February 27, 2004 provided additional data regarding two patients diagnosed with Alzheimer's disease (AD) and MCI/ borderline AD, which demonstrated "that the AD patients lymphocytes showed

a significant increase in the expression of IRP-2, up to 10-fold in one patient, although even the four-fold difference seen in the other patient is significant" (section 8 on page 3 of the Declaration).

The instant claims 7-9 encompass a method of identifying a subject as likely to develop or have AD or MCI by comparing amounts of probe that interact with IRP-2 in a sample of peripheral blood cells, wherein more probe that interacts with IRP-2 leads to identification of a subject as likely to develop or have AD or MCI. First, the instant specification, as originally filed, fails to present any information regarding this particular relationship between the level of expression of IRP-2 in peripheral blood cells in AD or MCI patients and unaffected individuals. Moreover, the claims clearly recite the limitation "more probe" as being indicative of AD or MCI. "More" is a relative term, therefore, in order to practice the instant invention without undue experimentation a point of reference, such as level of a probe which correlates to normal, AD or MCI-free, value must be disclosed. There also appears to be lack of information regarding how much "more" is indicative of AD or MCI because the instant specification does not disclose any quantitative data that is critical for practicing the instant method, as currently claimed.

Furthermore, the claims recite the limitation "identifying a subject as likely to develop [...] Alzheimer's disease", thus, claiming a method, which allows to predict a likelihood of developing AD. Because the instant specification does not present any information or working examples that would support or provide guidance on how to practice the claimed method to predict the development of AD or MCI in an individual by assessing the level of expression of IRP-2, a skilled artisan would have to resort to a

significant amount of undue experimentation to practice the full scope of the Applicant's invention.

Claim 21 is directed to a method for the identification of a defect in iron metabolism in a patient by detecting more or less probe that interacts with IRP-2 in a sample of peripheral blood cells as compared to control sample. The instant specification describes a working hypothesis that mutations in the IRP-2 gene or different expression of IRP-2 could be associated with diseases of neurodegenerative etiology. However, it is well known in the art that "iron metabolism" is not limited to or solely defined by IRP-2. Because the art does not recognize IRP-2 as being exclusively associated with iron metabolism, a skilled practitioner would have to rely only on the disclosure presented by Applicant to practice the instant invention. However, the instant specification presents no information regarding levels of a probe that correlates to a control, non-defective iron metabolism as well as to "a defect in iron metabolism". There are also no working examples that would guide and help a skilled practitioner to practice the claimed method.

Thus, for reasons explained above the Declaration of Kirsch is found to be insufficient to overcome the rejection of the instant pending claims.

In view of the lack of teachings and unpredictability of the art set forth earlier, and also the total absence of the working examples, the instant specification is not found to be enabling for a method of identifying a subject as likely to develop or have AD or MCI or to identify a defect in iron metabolism by comparing amounts of probe that interacts with IRP-2 in a sample of peripheral blood cells. It would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to use Applicant's invention as currently claimed.

Claim Rejections - 35 USC § 112

8. Claims 7-9 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claims 7 and 21 are vague and indefinite in so far as they employ the term "mutant IRP-2" as a limitation. This term is appears to be novel, and without a reference to a precise amino acid sequence identified by a proper SEQ ID NO: one cannot determine the metes and bounds of "mutant IRP-2". Moreover, because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a "mutant IRP-2", an artisan cannot determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation.

10. Claims 7 and 21 recite the limitation "protein". There is insufficient antecedent basis for this limitation within the claims. For example, claim 21 recites "sample having protein", "mutant IRP-2 protein" and "the protein in the biological sample". It is confusing and indefinite which proteins are intended by the claim. Clarification is required.

Furthermore, because the claimed method recites a step in which a probe that interacts with wild type IRP-2 or mutant IRP-2 is contacted with "protein", it is not obvious and cannot be determined from the claims "more" of which probe identifies the subject. Is it a probe that interacts only with wild type IRP-2, or with both (or more) forms of IRP-2 combined?

11. Claims 7 and 21 are indefinite as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: measuring the amount of probe detected after contacting the sample with the probe. Because the last step of the claimed methods clearly contains quantitative limitations, such as "more probe" or "more or less probe", the claimed methods appear to be not completed without the step that determines the amount of the probe.

12. Claims 8-9 are indefinite for being dependent from indefinite claim.

Conclusion

13. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If

Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (571) 273-0870. Official papers should NOT be faxed to (571) 273-0870.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Olga N. Chernyshev, Ph.D.

OLGA N. CHERNYSHEV, PH.D.
PATENT EXAMINER